

## Review on sedation for gastrointestinal tract endoscopy in children by non-anesthesiologists

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### Abstract

**AIM:** To present evidence and formulate recommendations for sedation in pediatric gastrointestinal (GI) endoscopy by non-anesthesiologists.

**METHODS:** The databases MEDLINE, Cochrane and EMBASE were searched for the following keywords "endoscopy, GI", "endoscopy, digestive system" AND "sedation", "conscious sedation", "moderate sedation", "deep sedation" and "hypnotics and sedatives" for publications in English restricted to the pediatric age. We searched additional information published between

January 2011 and January 2014. Searches for (upper) GI endoscopy sedation in pediatrics and sedation guidelines by non-anesthesiologists for the adult population were performed.

**RESULTS:** From the available studies three sedation protocols are highlighted. Propofol, which seems to offer the best balance between efficacy and safety is rarely used by non-anesthesiologists mainly because of legal restrictions. Ketamine and a combination of a benzodiazepine and an opioid are more frequently used. Data regarding other sedatives, anesthetics and adjuvant medications used for pediatric GI endoscopy are also presented.

**CONCLUSION:** General anesthesia by a multidisciplinary team led by an anesthesiologist is preferred. The creation of sedation teams led by non-anesthesiologists and a careful selection of anesthetic drugs may offer an alternative, but should be in line with national legislation and institutional regulations.

**Key words:** Gastro-intestinal endoscopy; Gastroscopy; Colonoscopy; Sedatives; Pediatric ages; Anesthetics; Analgesics

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**Core tip:** Sedation for pediatric gastro-intestinal endoscopy is preferably performed by pediatric anesthesiologists, as part of a multidisciplinary team. However, in many hospitals pediatric anesthesiology is insufficiently developed. The creation of sedation teams led by non-anesthesiologists and a careful selection of anesthetic drugs may offer an effective and safe alternative. These teams should be in line with national legislation and institutional regulations. This paper will help non-anesthesiologists to provide as good-as-possible sedation for children undergoing endoscopy. Practical protocols were developed providing up-to-date information on the most effective and most safe options.

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## INTRODUCTION

Esophago-gastro-duodenoscopy in children needs almost always to be performed under anesthesia or deep sedation. Procedural analgesia and sedation for procedures performed in ambulatory care are changing. The authors reviewed the literature on sedation and for endoscopy by non-anesthesiologists and to propose

practical algorithms.

In order to obtain the greatest yield from a pediatric gastrointestinal (GI) endoscopic procedure and to perform these with the highest quality and with the maximum level of safety, some prerequisites must be fulfilled. A pediatric gastroenterologist or dedicated pediatrician must have judged the necessity of the procedure to optimize patient management. The procedure must be performed by a skilled endoscopic team with appropriate equipment in a suitable environment. The patient and parents or guardians must be informed as much and good as possible.

General anesthesia is only possible in a limited number of centers because of shortness of anesthesiologists. The aim of this review is to present and discuss different sedation protocols for non-anesthesiologists for pediatric GI endoscopies. Several protocols for procedural sedation by non-anesthesiologists have been produced by different professional bodies and organizations. However, practical algorithms for these procedures have not been published<sup>[1]</sup>.

## MATERIALS AND METHODS

The search for studies on pediatric sedation for GI endoscopy was an update of van Beek and Leroy<sup>[2]</sup>'s search strategy for the period between January 2011 (when their search was finished) and January 2014 and utilized the following databases: MEDLINE, Cochrane, and EMBASE<sup>[2]</sup>. These were searched for the keywords "endoscopy, GI", "endoscopy, digestive system" and "sedation", "conscious sedation", "moderate sedation", "deep sedation", and "hypnotics and sedatives" for publications in English restricted to the pediatric age group, which was defined as 0 to 18 years. Subsequently a search for pediatric GI endoscopy sedation guidelines for the same keywords as above for the last 20 years with the same limits (publications in English, pediatric population) was undertaken. The search was expanded to include guidelines for GI endoscopy sedation by non-anesthesiologists for the adult population for the last 10 years. Furthermore a search for guidelines for pediatric procedural sedation published in the last 10 years was made.

## RESULTS

The first search revealed 12 studies of which 8 are listed in Table 1<sup>[3-10]</sup>. Four of them were not relevant: Liu *et al.*<sup>[11]</sup> analyzed anesthesia for outpatient gastroscopies and colonoscopies in adults only, Yen *et al.*<sup>[12]</sup> studied sex differences in sedation with midazolam and alfentanil for gastroscopy only in adults, too<sup>[3,4]</sup>. The aim of the study of Vadlamudi *et al.*<sup>[13]</sup> was evaluation of ileoscopy *via* stoma and not a sedation<sup>[13]</sup>. And finally, Siwiec *et al.*<sup>[14]</sup> tested transnasal gastroscopy with ultrathin endoscope in non-sedated healthy volunteers or patients with the signs or symptoms of gastro-esophageal reflux disease.

We found one guideline for pediatric GI endoscopy in

**Table 1** Publications from the first search (“endoscopy, gastrointestinal”, “endoscopy, digestive system” and “sedation”, “conscious sedation”, “moderate sedation”, “deep sedation”, and “hypnotics and sedatives”; limits: publications in English, paediatric population)

Ref.	Methodology	Results	Limitations	Conclusions
Bedirli <i>et al</i> <sup>[3]</sup>	<p>Study type: prospective, randomised, double-blinded</p> <p>Patients: N = 80; 1–16 yr; ASA I, II</p> <p>Procedure: upper GI endoscopy</p> <p>Drugs: baseline: propofol (1 mg/kg; additional 0.5–1 mg/kg as needed); intervention: fentanyl (2 µg/kg) <i>vs</i> tramadol (2 mg/kg)</p> <p>Intended sedation level: deep sedation</p> <p>Additional interventions: spray of lidocaine 10%; infusion of 10 lactated Ringer’s solution (10 mL/kg per hour); supplemental oxygen 3–4 L/min</p> <p>Administered by: anesthesiologist</p> <p>Outcome measures:</p> <p>Adverse events: HR (change for 20% from the baseline), BP (change for 20% from the baseline), SpO<sub>2</sub> (&lt; 90% for more than 15 s), respiratory rate, agitation score</p> <p>Effectiveness: Ramsey sedation score, duration of endoscopy, Steward recovery score, endoscopist’s rating of ease of procedure, total propofol consumption</p>	<p>Adverse events: self-limited bradycardia and transient desaturation in age group 0–2 yr, more in the fentanyl group</p> <p>Effectiveness: lower sedation scores in tramadol group; no difference of gastroenterologist rating</p>	<p>Only one dosage of drugs instead of titrating them</p>	<p>Propofol with tramadol or propofol provided efficient sedation; significantly less adverse effects in the tramadol group</p>
Brecelj <i>et al</i> <sup>[4]</sup>	<p>Study type: randomized, controlled, single-blinded</p> <p>Patients: N = 201; 1–18 yr</p> <p>Procedure: gastroscopy, colonoscopy</p> <p>Drugs: ketamine (0.75 mg/kg with additions of 0.25 mg/kg up max. to 1.5 mg/kg; repeated after 10–15 min at 0.5 mg/kg as needed)</p> <p>Intervention: midazolam (0.1 mg/kg; max 2.5 mg; repeated after 30–60 min at 0.05 mg/kg as needed) <i>vs</i> no premedication</p> <p>Intended sedation level: deep sedation</p> <p>Additional interventions: none</p> <p>Administered by: dedicated nurse under supervision of endoscopist</p> <p>Outcome measures:</p> <p>Adverse events: respiration rate, HR, BP, SaO<sub>2</sub> (any drop below 92%), adverse reactions</p> <p>Effectiveness: ease of procedure, total ketamine consumption</p>	<p>Adverse events: mild self-limited laryngospasm in 3%, high rate of desaturations (approx. in 40%), vomiting in 17%, regardless of study group; more emergence reactions in ketamine group during recovery (10 <i>vs</i> 2)</p> <p>Effectiveness: high rate of sedation adequacy</p>	<p>Study was not double-blinded</p>	<p>Ketamine starting dose should be at least 1 mg/kg; more emergence reactions without midazolam premedication; same frequency of other adverse reactions</p>
Miqdady <i>et al</i> <sup>[5]</sup>	<p>Study type: retrospective cohort study</p> <p>Patients: N = 301; 1 (more than 10 kg)–18 yr; ASA I, II</p> <p>Procedure: upper, lower or combined GI endoscopy</p> <p>Drugs: atropine (0.01–0.02 mg/kg per minute; 0.1 mg, max. 0.4 mg); midazolam (0.05–0.2 mg/kg); ketamine (0.5–1 mg/kg)</p> <p>Intended sedation level: deep sedation</p> <p>Additional interventions: none</p> <p>Administered by: endoscopist</p> <p>Outcome measures:</p> <p>Adverse events: respiration rate, HR, BP, SaO<sub>2</sub> (any drop below 94%), side effects</p> <p>Effectiveness: the adequacy of sedation</p>	<p>Adverse events: desaturation in 12.3%, in 1.2% disruption of examination due to persistent desaturation; in 1.2% respiratory distress after examination</p> <p>Effectiveness: effective and uneventful sedation in 79.4%</p>	<p>Retrospective study</p>	<p>Midazolam and ketamine sedation is safe and effective for diagnostic GI endoscopies in children older than 1 yr weighting more than 10 kg without comorbidities</p>

Motamed <i>et al</i> <sup>[6]</sup>	<p>Study type: prospective, randomised, double-blinded</p> <p>Patients: N = 150; 1–18 yr; ASA I, II</p> <p>Procedure: upper GI endoscopy</p> <p>Drugs: main sedative: midazolam (0.1 mg/kg; if needed repeated doses up to 5 mg or 0.3 mg/kg); premedication 45 min before the procedure with oral placebo (normal saline), oral ketamin (5 mg/kg), or oral fentanyl (2 µg/kg)</p> <p>Additional interventions: spray of lidocaine 10%; additional oxygen through nasal cannula at 2 L/min</p> <p>Administered by: registered nurse supervised by anaesthesiologist</p> <p>Outcome measures:</p> <p>Adverse events: respiration rate, HR (decrease by 30% from baseline), BP (decrease or increase by 20%), SaO<sub>2</sub> (any drop below 90%)</p> <p>Effectiveness: total midazolam dose, modified Ramsay sedation score, procedure time, discharge time, ease of <i>in situ</i> catheter placement, separation from parents agitation, the adequacy of sedation</p>	<p>Adverse events:</p> <p>in total in 26% of patients (hypoxia in 7.3%, hypotension in 6.7%, dizziness in 20%, nausea in 10%, vomiting in 17.6%); mild, easily managed</p> <p>Effectiveness:</p> <p>the total recovery and procedure duration time was shorter in the ketamine-midazolam group, inadequate sedation in 10.2% in placebo-midazolam and in 8% in fentanyl-midazolam <i>vs</i> in 3.9% in ketamine-midazolam group; the mean administered dose of midazolam was the lowest in ketamine-midazolam group; the <i>in situ</i> line placement and separation from parents was easier in ketamine-midazolam group; only 27.4% of patients did not remember the procedure</p>	<p>Sedation with oral ketamine-iv midazolam is better than placebo-midazolam or oral fentanyl-iv midazolam</p>
Chiaretti <i>et al</i> <sup>[7]</sup>	<p>Study type: retrospective (12 yr), multicentric</p> <p>Patients: N = 36516; 1 &gt; 10 yr; ASA I, II, III</p> <p>Procedure: different painful procedures</p> <p>Drugs: main sedative: propofol 2 mg/kg in children from 1 to 8 yr of age and 1 mg/kg in older children and in children younger than 1 yr; further doses of 0.5–1.0 mg/kg in the case of agitation or complain; premedication: atropine 0.010–0.015 mg/kg, ketamine (0.5 mg/kg) to avoid infusion pain in 2 centres (not in gastroscopy); additional oxygen through nasal cannula at 6 L/min</p> <p>Intended sedation level: deep sedation</p> <p>Administered by: paediatrician (anaesthesiologist available in case of need)</p> <p>Outcome measures: mean arterial pressure, heart rate and SatO<sub>2</sub>, incidence, type and timing of adverse events (major and minor) and number of calls to the emergency team</p> <p>Effectiveness: total dosage of the sedative agents, level of sedation (Ramsay scale)</p>	<p>Adverse events:</p> <p>in 6 patients (0.02%) emergency team intervention (prolonged laryngospasm in 3 patients, bleeding in 1, intestinal perforation in 1, and 1 during lumbar puncture); milder adverse events: hypotension in 19 patients (0.05%), ventilation by face mask and additional oxygen in 128 patients (0.4%), laryngospasm in 78 patients (0.2%), bronchospasm in 15 patients (0.04%); minor complications more often in children who underwent gastroscopy; none of the children experienced severe side effects or prolonged hospitalisation</p>	<p>Retrospective study</p> <p>Propofol is safe and effective for paediatrician-administered procedural sedation in children; appropriate training for paediatricians is important</p>
Gül <i>et al</i> <sup>[8]</sup>	<p>Study type: randomized, controlled, double-blinded</p> <p>Patients: N = 64; 3–14 yr; ASA I</p> <p>Procedure: esophagogastroduodenoscopy</p> <p>Drugs: main sedative: propofol 2 mg/kg; analgesic: group R: remifentanyl 0.25 µg/kg, group F: fentanyl 0.5 µg/kg; additional oxygen through nasal cannula at 4 L/min</p> <p>Intended sedation level: deep sedation</p> <p>Administered by: anesthesiologist</p> <p>Outcome measures: MAP, HR, RR, and SpO<sub>2</sub></p> <p>Effectiveness: ease of gastroscopy, patient's movements during procedure, additional doses of drugs; level of sedation (Ramsay scale); duration of PACU stay</p> <p>Study type: retrospective analysis of prospectively collected data</p> <p>Patients: N = 4904; 15–90 yr; ASA I–IV</p> <p>Procedure: esophagogastroduodenoscopy</p> <p>Drugs propofol 1–100 mg and/or midazolam 1–3 mg<sup>2</sup> mg/kg</p> <p>Administered by: endoscopist</p> <p>Outcome measures: influence of pre-existing disease and ASA score on oxygen desaturation (SpO<sub>2</sub>) &lt; 90%</p>	<p>Adverse events:</p> <p>prolonged apnoea in 14 (43.8%) children in group R and in 11 (33.3%) children in group F; none required endotracheal intubation;</p> <p>Effectiveness</p> <p>intraoperative respiratory rate, time to eye opening, opioid consumption, and duration of recovery were significantly shorter in group R than in group F</p> <p>duration of PACU stay were significantly shorter in group R than in group F</p> <p>Adverse events:</p> <p>hypoxemia in 245 patients (5%); risk factors: high BMI (30 kg/m<sup>2</sup>), hypertension, diabetes, gastrointestinal disease, heart disease</p> <p>ASA score was not predictive for hypoxemia</p>	<p>Retrospective study</p> <p>Remifentanyl (combined with propofol) is an efficient and as safe as fentanyl propofol combination for esophagogastroduodenoscopy in children</p> <p>Independent risk factors for hypoxemia were high BMI, hypertension, diabetes, gastrointestinal and heart diseases and combined gastro and colonoscopy</p>
Long <i>et al</i> <sup>[9]</sup>			



Agostoni <i>et al</i> <sup>[10]</sup>	<p>Study type: retrospective analysis of prospectively collected data</p> <p>Patients: N = 17999 (17524 in older than 12 yr, 457 in &lt; 12 yr); 4-74 yr; ASA I-IV</p> <p>Procedure: esophagogastroduodenoscopy and in some cases different procedures (mucosectomy, hemostatic clip, percutaneous endoscopic gastrostomy, ...)</p> <p>Drugs: propofol induction (in children 1-2 mg/kg BW) then in continuous infusion</p> <p>Intended sedation level: deep sedation</p> <p>Administered by: anesthesiologist</p> <p>Outcome measures: adverse events (hypotension, desaturation, bradycardia, hypertension, arrhythmia, aspiration, respiratory depression, vomiting, cardiac arrest, respiratory arrest, angina, hypoglycemia, and/or allergic reaction)</p>	<p>Adverse events:</p> <p>rare in children (2.6%) and in adults (4.5%), in children were more often only bradycardia (2.1%) and hypotension (0.44%)</p> <p>3 adult patients died; no death case in children</p>	<p>Retrospective analysis, single centre data</p>	<p>Deep sedation with intravenous propofol for endoscopic procedures is safe in children and adults</p>
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ASA: American Society for Anesthesiology; BP: Blood pressure; GI: Gastrointestinal; HR: Heart rate; SpO2: Oxygen saturation; BMI: Body mass index; RR: Respiratory rate.

### English which addressed different aspects including sedation<sup>[15]</sup>.

We expanded the search to guidelines for sedation for GI endoscopy performed by non-anesthesiologists in adult patients during the last 10 years. The search revealed 9 publications which are listed in Table 2<sup>[16-24]</sup>.

The search for guidelines for pediatric procedural sedation published in English during the last 10 years revealed 10 publications. Two are general guidelines for sedation in children<sup>[25,26]</sup>. Another one, followed by an update published 7 years later, addresses specifically ketamine sedation for emergency departments<sup>[27,28]</sup>. Others are specifically developed for sedation for dental procedures in children. They are listed in Table 3<sup>[15,25,26,28-33]</sup>.

### Pre-requisites for safe and effective sedation by non-anesthesiologists

GI endoscopy must be discussed with the child if emotionally and intellectually competent enough and parent(s)/guardian(s). The pre-sedation assessment is listed in Table 4. Patients should be classified by physical status assessment as developed by the American Society for Anesthesiology (ASA) (Table 5). If the child's ASA classification conforms to class I or II, sedation can be performed safely. If the child fits in ASA class III classification, the benefits of sedation must be carefully weighed against the risks and in the vast majority of cases anesthesiology will be preferable. Patients in ASA class IV and V must be anesthetized by anesthesiologists<sup>[28,34]</sup>.

The depth of sedation is influenced by the procedure. If analgesia is needed together with sedation, as in the case of endoscopic-therapeutic procedures, the patient has to be anesthetized. The same is valid for emergency GI endoscopies such as removal of a foreign body from the upper GI tract and GI bleeding. Sedation necessitates that a team member assigned for observing the vital signs of the patient, since monitoring of pulse oximetry, heart rate and preferably also capnography are insufficient<sup>[8,12]</sup>.

Equipment for resuscitation must be present in the endoscopy room. The team has to be trained in pediatric advanced life support techniques and has to be familiar with measures needed in any scenario of complications<sup>[1]</sup>.

### Sedatives and their combinations

Legislation and regulation regarding limitations of administration of different medications, such as inhalation anesthetics, differ from country to country. Therefore, limitations caused by local legislation should be carefully checked. In most countries, the administration of inhalation anesthetics is only authorized by anesthesiologists.

### Premedication

Premedication with midazolam (oral or intra-nasal) lessens the stress for an intravenous (iv) catheter placement and other preparations for GI endoscopy before sedation or anesthesia. This procedure is effective and safe although intranasal administration may cause local discomfort. In order to decrease the stress and pain caused by a venepuncture, an eutectic mixture of the topical anesthetics lidocaine and prilocaine provides local anesthesia when applied with an occlusive dressing 30-60 min before venipuncture<sup>[35]</sup>.

An iv catheter provides the most effective way of delivering agents needed for sedation and analgesia. Inhalation, intramuscular or other sedation regimens are less well

**Table 2 Gastrointestinal endoscopy sedation guidelines for adults**

Organisation Ref.	Title	Year of publication
American Association for the Study of Liver Diseases; American College of Gastroenterology; American Gastroenterological Association Institute; American Society for Gastrointestinal Endoscopy; Society for Gastroenterology Nurses and Associates Vargo <i>et al</i> <sup>[16]</sup>	Multisociety sedation curriculum for GI endoscopy	2012
Task Force Members. European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology Dumonceau <i>et al</i> <sup>[17]</sup>	Guideline: Non-anesthesiologist administration of propofol for GI endoscopy	2010
Society of American Gastrointestinal Endoscopic Surgeons Heneghan <i>et al</i> <sup>[18]</sup>	Surgeons. Society of American Gastrointestinal Endoscopic Surgeons guidelines for office endoscopic services	2009
Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy Lichtenstein <i>et al</i> <sup>[19]</sup>	Sedation and anesthesia in GI endoscopy	2008
Training Committee of the American Society for Gastrointestinal Endoscopy Vargo <i>et al</i> <sup>[20]</sup>	Training in patient monitoring and sedation and analgesia	2007
Working Group on Endoscopy, Austrian Society of Gastroenterology and Hepatology (OGGH) Schreiber <sup>[21]</sup>	Austrian Society of Gastroenterology and Hepatology (OGGH)-guidelines on sedation and monitoring during GI endoscopy	2007
Training Committee American Society for Gastrointestinal Endoscopy <sup>[22]</sup>	Training guideline for use of propofol in gastrointestinal endoscopy	2004
American Society for Gastrointestinal Endoscopy, Standards of Practice Committee Waring <i>et al</i> <sup>[23]</sup>	Guidelines for conscious sedation and monitoring during GI endoscopy	2003
Standards Practice Committee American Society for Gastrointestinal Endoscopy Faigel <i>et al</i> <sup>[24]</sup>	Guidelines for the use of deep sedation and anesthesia for GI endoscopy	2002

GI: Gastrointestinal.

**Table 3 Paediatric procedural sedation guidelines**

Organisation Ref.	Title	Year of publication
Green <i>et al</i> <sup>[28]</sup>	Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update	2011
National Clinical Guideline Centre (United Kingdom) <sup>[26]</sup>	Sedation in children and young people: Sedation for diagnostic and therapeutic procedures in children and young people	2010
American Academy on Pediatric Dentistry Clinical Affairs Committee-Sedation and General Anesthesia Subcommittee; American Academy on Pediatric Dentistry Council on Clinical Affairs <sup>[29]</sup>	Guideline on use of anesthesia personnel in the administration of office-based sedation/general anesthesia to the pediatric dental patient	2009
American Academy on Pediatrics; American Academy on Pediatric Dentistry <sup>[30]</sup>	Guideline for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures	2009
American Academy of Pediatrics; American Academy of Pediatric Dentistry Coté <i>et al</i> <sup>[25]</sup>	Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update	2006
American Academy on Pediatric Dentistry Clinical Affairs Committee-Sedation and General Anesthesia Subcommittee; American Academy on Pediatric Dentistry Council on Clinical Affairs <sup>[31]</sup>	Guideline on use of anesthesia care providers in the administration of in-office deep sedation/general anesthesia to the pediatric dental patient	2005
American Academy of Pediatric Dentistry	Guideline on the elective use of minimal, moderate, and deep sedation and general anesthesia for pediatric dental patients	2005
American Academy of Pediatric Dentistry Committee on Sedation and Anesthesia <sup>[15]</sup>		
American Academy of Pediatric Dentistry <sup>[32]</sup>	Clinical guideline on the elective use of minimal, moderate, and deep sedation and general anesthesia for pediatric dental patients	2004
Green <i>et al</i> <sup>[27,28]</sup>	Clinical practice guideline for emergency department ketamine dissociative sedation in children	2004
UK National Clinical Guidelines in Pediatric Dentistry Hosey <sup>[33]</sup>	UK National Clinical Guidelines in Paediatric Dentistry. Managing anxious children: the use of conscious sedation in paediatric dentistry	2002

**Table 4 Preparation of a child for sedation for gastrointestinal endoscopy**

Preparation of the patient		Comments
Planning of the investigation / procedure	Understanding of the investigation	Explanation of the examination: Aims of investigation Possible risks
	Informed consent Presedation assessment	Signed by parents and/or the child (depending on the age and legislation) Co-morbidity ASA score (Table 5) Medicines Bleeding tendency Previous undesirable effects of sedation/anesthesia Specific contraindications for the planned sedation Previous complications of investigations Allergies The need for antibiotic prophylaxis Laboratory investigation/consultation before the investigation/procedure ( <i>e.g.</i> , tests of hemostasis in case of bleeding tendency) Additional important data
Preparation On the day of examination	Exact instructions (fasting time, colon cleansing <i>etc.</i> )	
	Focused history:	
	Current health state	
	Infectious diseases	
	Epidemiologic situation	
	Fasting	
	Allergy	
	Specific contraindications for the planned sedation	
	Physical examination	Complete physical examination with the focus on respiratory and cardiovascular system
	Measurement of vital signs	Arterial blood pressure Heart rate
	Laboratory investigations	Arterial oxygen saturation If needed

ASA: American Society for Anesthesiology.

**Table 5 American Society of Anesthesiologists physical status classification<sup>[24]</sup>**

Class	Description	Suitability for sedation
Class I	A normally healthy patient	Excellent
Class II	A patient with mild systemic disease ( <i>e.g.</i> , controlled asthma)	Generally good
Class III	A patient with severe systemic disease ( <i>e.g.</i> , a child who is actively wheezing)	Intermediate to poor
Class IV	A patient with severe systemic disease that is a constant threat to life ( <i>e.g.</i> , a child with status asthmaticus)	Poor
Class V	A moribund patient who is not expected to survive without the operation ( <i>e.g.</i> , a patient with severe cardiomyopathy requiring heart transplantation)	Extremely poor

documented. An *iv* catheter is also important for emergency access in the case of adverse events occurring during sedation or the endoscopic procedure<sup>[25,36,37]</sup>.

Mechanisms of action and the main undesirable effects of sedatives and adjuvant medicines are listed in Table 6<sup>[8,38-49]</sup>. Usual dosage regimens and the main contraindications are listed in Table 7.

### Propofol

Propofol is a rapid onset and short acting anesthetic without analgesic properties and with a narrow therapeutic range. Its sedative properties result from agonistic action on gamma-aminobutyric acid (GABA) receptors. Propofol is contraindicated in infants younger than 1 mo because of missing data on safety according to a Cochrane review<sup>[50]</sup>. The main undesirable effects include

pain on injection, respiratory depression, bradycardia and hypotension<sup>[38,46]</sup>.

van Beek and Leroy<sup>[2]</sup> reported failure to conduct a procedure due to incomplete sedation in only 0.0%–0.4% of cases, despite the fact that the sedation was performed in 88.1% by non-anesthesiologists<sup>[2]</sup>. The recovery time after propofol administration was shorter than after midazolam/meperidine<sup>[2]</sup>. Major respiratory complications occurred in 11/3883 propofol sedations (0.3%), but no intubation and no sequelae were reported. The incidence of undesirable effects (*e.g.*, temporary desaturation due to hypoventilation, laryngospasm) was comparable to other protocols and was more frequent in younger children, especially infants<sup>[2]</sup>.

A randomized study in 90 adults undergoing colonoscopy showed that the satisfaction of patients was greater

**Table 6 Sedatives and adjuvant medicines for paediatric gastrointestinal endoscopy sedation**

Generic name	Mechanism(s) of action	Main undesirable effects	Comments	Ref.
<b>Sedatives</b>				
Fentanyl	Opioid receptors agonist; analgesia and sedation	Respiratory depression, hypotension	Due to analgesic effect only it should be combined with benzodiazepine; antagonist naloxone	[38-40]
Ketamine	Binds to the Nmethyl-Daspartate (NMDA) receptors; anesthesia, analgesia, amnesia, sedation, immobilisation	Laryngospasm, hypertension, tachycardia, hypersalivation, vomiting, random movements, increase in intraocular pressure, emergence phenomena (floating sensations, vivid dreams, blurred vision, hallucinations, and delirium)	Beneficial respiratory properties and analgesic potency S(+) isomer has less adverse effects	[40-42]
Meperidine	Opioid receptors agonist; analgesia and sedation	Respiratory depression, pruritus, vomiting	Interaction with monoamine oxidase inhibitors	[38,43,44]
Midazolam	GABA receptor agonist; anterograde amnesia, anxiolysis, sedation, hypnosis	Respiratory depression, hypotension, paradoxical agitation	Without analgesic effect; should be combined with analgesic (usually opioids)  Concomitant use with opioid increases the risk of respiratory depression antagonist flumazenil	[38-40]
Nitrous oxide	Inhalation anaesthetic	Vomiting, dizziness, voice change, euphoria, laughter	The need of scavenging system Use mostly limited to anaesthesiologists	[38,40,45]
Propofol	GABA receptor agonist; sedation, hypnosis, amnesia	Respiratory depression, apnoea, hypotension, painful injection		[38,40,46]
Sevoflurane	Inhalation anaesthetic	Recovery agitation, bradycardia, hypotension, cough, vomiting, seizures	The need of scavenging system Use limited to anaesthesiologists	[47-49]
<b>Antagonists</b>				
Flumazenil	Benzodiazepine antagonist	Nausea, vomiting	Contraindicated in benzodiazepine dependence, seizure disorder, cyclic antidepressant overdose, elevated intracranial pressure in patients, and in patients taking medicines known to lower the seizure threshold	[40]
Naloxone	Opioid antagonist	Nausea, vomiting, tachycardia		[40]

and there were less undesirable effects when they were sedated by an endoscopist than by an anesthesiologist<sup>[51]</sup>. A Scandinavian study tested a 6-wk educational program for registered nurses with excellent safety results<sup>[52]</sup>.

The largest multicenter prospective study of propofol sedation for different pediatric procedures outside an operating theatre was published by the international (United States and Canada) Pediatric Sedation Research Consortium. They analysed the data of 49836 propofol sedation episodes and showed that propofol-based sedation is amongst the safest sedation practice for children<sup>[53]</sup>. Cardio-respiratory resuscitation was necessary in two cases. Pulmonary aspiration of gastric fluid secondary to vomiting during sedation occurred in four patients. Less serious respiratory adverse events were: desaturation in 154/10000 procedures; central apnea or upper airway obstruction in 124/10000; stridor in 10/10000; laryngospasm in 20/10000; excessive salivation in 73/10000; and vomiting in 10/10000 cases. The authors of this report estimate propofol sedation safe in children. Interestingly there were no differences in adverse effects between anesthesiologists and non-anesthesiologist. However, it should be pointed out that this report did not focus on upper GI endoscopy specifically, in which a shared airway is an important consideration, especially as attempting esophageal intubation may have the potential for induction of laryngospasm. However,

it is stressed by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Endoscopy Working Group that the advice of the Pediatric Sedation Research Consortium, including institutions with highly motivated and well organized sedation/anesthesia teams, is only to be considered when anesthetic teams are not available, and that priority should go to actions to obtain these anesthetic teams.

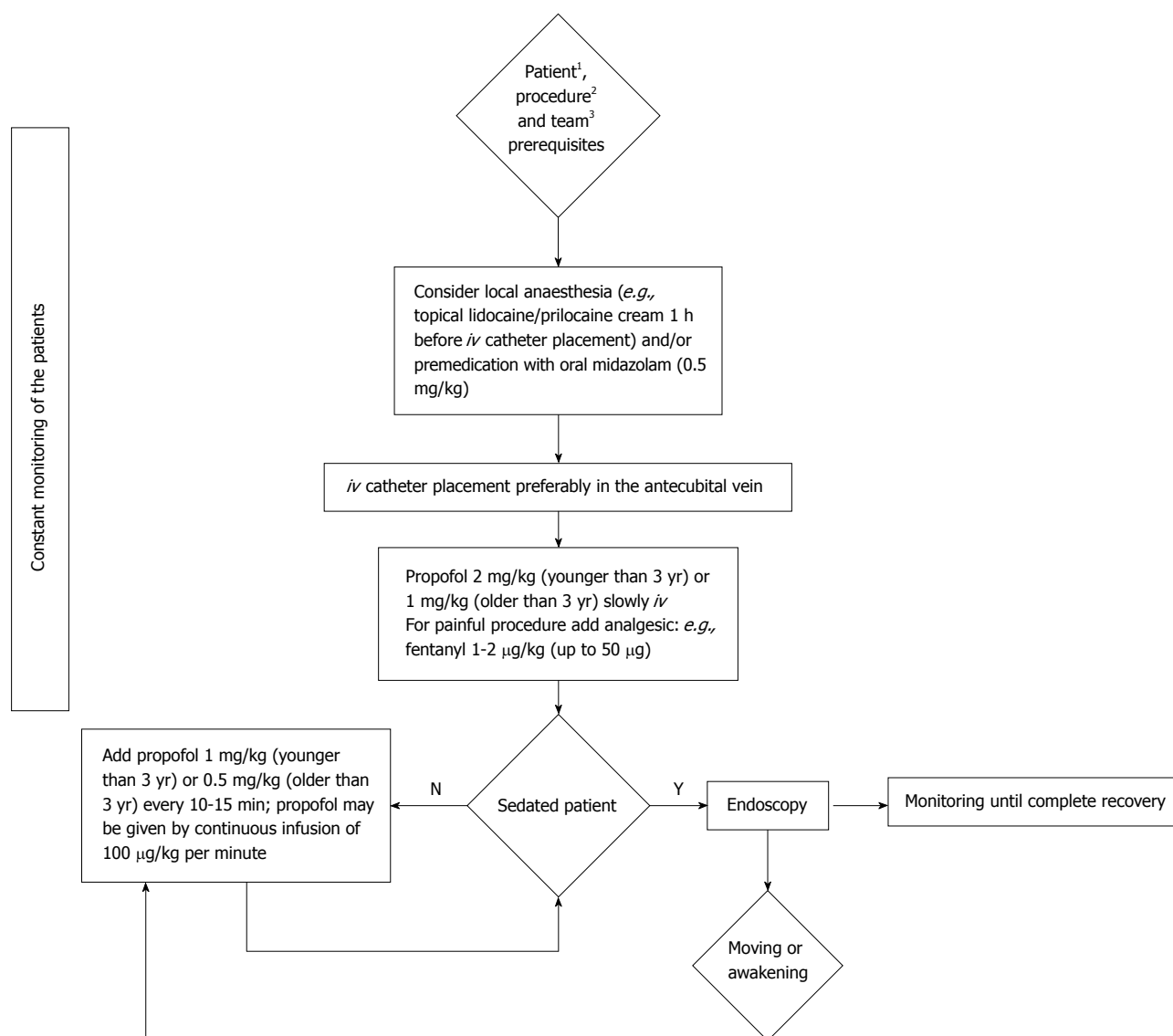
Chiaretti *et al*<sup>[7]</sup> published a retrospective study on pediatric procedural sedation with propofol over a 12-year period in three Italian hospitals<sup>[7]</sup>. They analyzed 36516 procedural sedations for different painful procedures. Deep sedation was achieved in all patients. None of the children experienced severe side effects or needed a prolonged hospitalization. In six patients (0.02%) emergency team had to intervene (prolonged laryngospasm in three patients, bleeding in one, intestinal perforation in one, and one during lumbar puncture). But milder adverse events were more often: hypotension in 19 patients (0.05%), ventilation by face mask and additional oxygen in 128 patients (0.4%), laryngospasm in 78 patients (0.2%), bronchospasm in 15 patients (0.04%). Minor complications were more often in children who underwent gastroscopy.

The usual loading dose of propofol is 2 mg/kg in infants and young children (younger than 3 years) and 1 mg/kg in older children and teenagers. Subsequent



Table 7 The list of sedatives/analgesic, adjuvant medicines and antagonists with usual dosage regimens, and main contraindications

Medicine generic name	Route	Dose	Time to start sedation/analgesia (after <i>iv</i> application)	Sedation/analgesia duration	Repeating time and dose	Contraindications	Comments	Ref.
Sedative/analgesic Fentanyl	<i>iv</i>	1–2 µg/kg (up to 50 µg)	0.5 s	20–40 min (30–60 min)	3 min 1–1.25 µg/kg 10 min 0.5 mg/kg	Severe cardiovascular disease, malignant hypertension, CSF obstructive states (controversial), intraocular pressure pathology; previous psychotic illness, hyperthyroidism or thyroid medicine use; porphyria	Due to higher clearance younger children need frequent dosing A single enantiomer S(+); the anesthetic management of seriously ill hypovolemic patients, it may be the agent of choice for managing children and burned patients; low cost	[38,40] [8,40–42]
Ketamine	<i>iv</i> slowly over 1 min; other routes have less predictive effects and different dosing – see the discussion	1–1.5 mg/kg	1–5 min	15 min		Simultaneous treatment with monoamine oxidase inhibitors		
Meperidine	<i>iv</i> slowly over 1–2 min	0.3–2 mg/kg	3–6 min	60–180 min		Respiratory depression, hypotension	Rarely used as a sole sedative; might be used to sedate the frightened child before <i>iv</i> catheter placement; mostly combined with opioids; paradoxical irritation in 1%–5% of patients	[38,43,44] [38–40]
Midazolam	<i>iv</i> slowly over 2–3 min; other routes have less predictive effects and different dosing	0.05–0.1 mg/kg in < 5 yr (max. 0.6 mg/kg); in 6–12 yr 0.025–0.05 mg/kg (max. 0.4 mg/kg); in older than 12 yr 2–2.5 mg (in total not per kg BW)	2–3 min	45–60 min	Repeating doses every 2–5 min until desired effect; in children 6 mo–5 yr total dose up to 0.6 mg/kg or max. 6 mg; in 6–12 yr total dose up to 0.4 mg/kg or max. 10 mg; in older than 12 yr additional boluses of 1 mg until desired sedation	Pneumothorax, bowel obstruction, head injury, pregnancy		
Nitrous oxide	Inhalation	Mostly the mixture of nitrous oxide (50%) and oxygen	0.5–1 min	5 min	Continuously or “on demand”		Its use limited to anaesthesiologists	[38,40,45]
Propofol	<i>iv</i>	2 mg/kg in infants and young children (younger than 3 yr); 1 mg/kg in children older than 3 yr	1–2 min	5–15 min	1 mg/kg (infants and children up to 3 yr); 0.5 mg/kg (children older than 3 yr) to reach the desired sedation; may be continuously infused at 100 µg/kg per min and increasing the speed of infusion by 50 µg/kg per min for prolonged procedures	Egg or soy allergy	For additional medication to alleviate infusion pain see text; alfentanil but not fentanyl increases propofol blood level; in many countries the use is limited to anaesthesiologists	[38,40,46] [47–49]
Sevoflurane	Inhalation	Different concentrations according to the age				Duchenne’s muscular dystrophy, moderate to severe liver disease of unknown aetiology, history of malignant hyperthermia	Its use limited to anaesthesiologists	
Antagonists Flumazenil	<i>iv</i>	0.02 mg/kg (max. 1 mg)	1–3 min	30 min	1 min; same dose	Chronic benzodiazepine use; ingestion of drugs that increase the risk for seizures development (e.g., cyclic antidepressants, cyclosporine, and others)	Due to its shorter duration of action than most of benzodiazepines (e.g., midazolam) repeated doses may be needed	[38,40]
Naloxone	<i>iv</i> or <i>i.m.</i>	0.1 mg/kg (max. 2 mg)	2 min	20–40 min	2 min; same dose	Hypersensitivity only	Due to its shorter duration of action than most of opioids (e.g., fentanyl) repeated doses may be needed	[38,40]



**Figure 1** Flow chart of propofol sedation protocol for paediatric gastrointestinal endoscopy. <sup>1</sup>Older than 1 mo, without contraindications (egg or soy allergy); <sup>2</sup>Diagnostic endoscopy or procedure for which no endotracheal intubation is needed; <sup>3</sup>The team qualified for paediatric sedation for gastrointestinal endoscopy.

boluses of 1 mg/kg for younger, or 0.5 mg/kg for older children, may be added to ensure the appropriate level of sedation. For longer procedures propofol may be administered in a continuous infusion<sup>[38]</sup>.

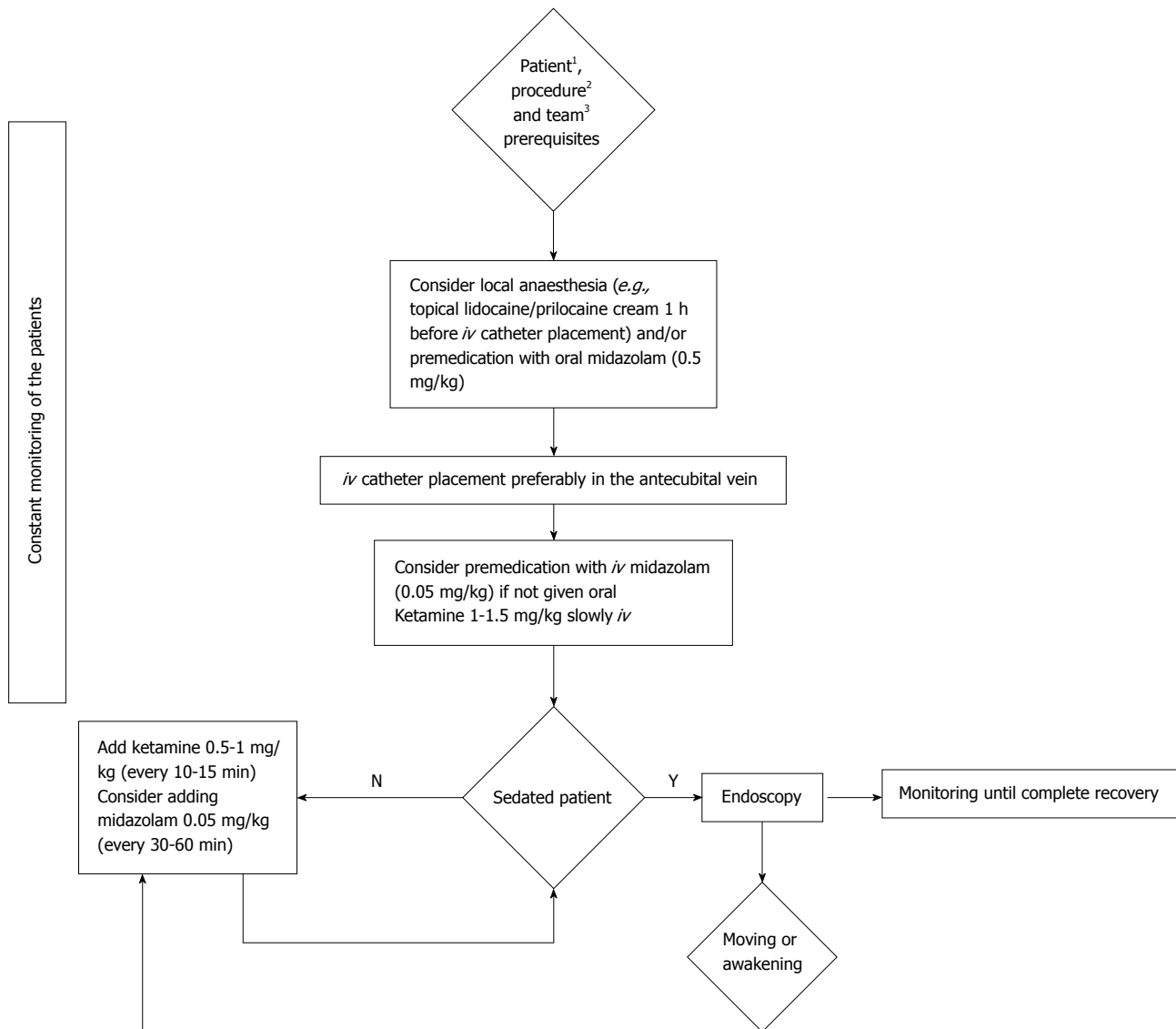
For painful procedures an analgesic must be added as propofol has no analgesic properties<sup>[38]</sup>. Bedirli *et al*<sup>[3]</sup> showed that the addition of tramadol or fentanyl to propofol provided efficient sedation, with less adverse events in the tramadol group (less desaturation, hypotension, and bradycardia; but more vomiting in fentanyl group)<sup>[3]</sup>. According to Gül *et al*<sup>[8]</sup> there was no difference in safety and efficacy between remifentanyl and fentanyl co-administration with propofol.

The pain of propofol injection can be reduced by choosing a larger vein such as the antecubital site, or alternatively the injection of lidocaine<sup>[54]</sup>. A possible flow chart of propofol sedation for pediatric GI endoscopy is presented in Figure 1.

Generally, one cannot extrapolate data from adult practice to children. However, four different European Societies (of Gastrointestinal Endoscopy, of Gastroenterology, of Endoscopy Nurses and Associates, and of Anesthesiology) jointly issued guidelines for propofol sedation of adults for GI endoscopy by non-anaesthesiologists<sup>[16]</sup>. It is interesting that although the Board of Directors of the European Society of Anesthesiology (ESA) decided unanimously to endorse these guidelines, a majority of the national societies of the ESA did not support them. Consequently ESA retracted the endorsement<sup>[55]</sup>. The Danish training program for nurses includes training on how to administer propofol for GI endoscopic procedures in adults<sup>[52]</sup>.

### Ketamine

Ketamine is a dissociative anesthetic and analgesic. It is an N-methyl-D-aspartate channel antagonist and



**Figure 2** Flow chart of ketamine sedation protocol for paediatric gastrointestinal endoscopy. <sup>1</sup>Older than 3 mo, without contraindications (severe cardiovascular disease, malignant hypertension, CSF obstructive states, intraocular pressure pathology, psychotic illness, hyperthyroidism or thyroid medicines use, and porphyria); <sup>2</sup>Diagnostic endoscopy or procedure for which no endotracheal intubation is needed; <sup>3</sup>The team qualified for paediatric sedation for gastrointestinal endoscopy.

depresses sensory association areas of the cortex, limbic system and thalamus. It has been used for a long time for sedation and analgesia in emergency pediatrics due to its association with a preserve gag reflex and lack of respiration depression and hypotension<sup>[41]</sup>. Despite its good safety profile, the significant association with laryngospasm (especially with gastroscopy), emergence phenomena such as hallucinations, excitation, nightmares, delirium, recurrent illusions or “flashbacks”, vomiting, and hypersalivation limit ketamine’s broader use<sup>[27,38,41]</sup>.

When used as a sedative, ketamine must be administered by slow *iv* injection at a dosage of 1-2 mg/kg initially. The sedative effect lasts 10-15 min. Repeated doses of 0.5 mg/kg prolong its action (Figure 2)<sup>[27,38]</sup>.

The most frequent undesirable effects are vomiting, hypersalivation, nystagmus, hypertension, tachycardia,

skin erythema, and emergence phenomena. Laryngospasm, which is potentially of greatest danger, is uncommon. The use of ketamine is contraindicated in infants younger than 3 mo, patients with psychosis, uncontrollable hypertension or hyperthyroidism, and as it increases intracranial and intraocular pressure. Ketamine should not be used after a head or eye trauma, or surgery, although some data advocate against these precautions<sup>[27,38]</sup>.

The concomitant use of midazolam with ketamine decreases the frequency of emergence phenomena, although this remains controversial<sup>[56]</sup>. Two randomized double-blind studies performed in pediatric emergency departments did not find sufficient evidence to support the addition of midazolam for this purpose<sup>[57,58]</sup>. However, a randomized study using midazolam in co-administration with ketamine for pediatric sedation for GI endoscopy

suggests that midazolam does prevent emergence phenomena<sup>[4]</sup>. Other co-administered medicines might lessen some undesirable effects of ketamine but their use is not supported by sufficient evidence. Anticholinergics may prevent hypersalivation<sup>[59]</sup>, but this has also been contradicted<sup>[60]</sup>. The anti-emetic ondansetron prevents vomiting in some patients<sup>[61]</sup>.

### **Benzodiazepines and opioids**

Midazolam is a short-acting benzodiazepine which is widely used for sedation but is generally considered to be insufficient as a monotherapy. It has anxiolytic, amnesic, sedative, hypnotic, muscle relaxant, and anticonvulsant properties which result from GABA receptor activation<sup>[38,39]</sup>. The major undesirable effects are respiratory depression and hypotension, which are avoidable with appropriate dosing and are reversed by the antagonist flumazenil<sup>[38]</sup>. Other undesirable effects such as paradoxical agitation are reported in up to 15% of children<sup>[38]</sup>.

Midazolam may be administered orally as an anxiolytic before the placement of an *iv* cannula but its effect is less predictive orally than when administered *iv*. The usual starting dose is 0.1 mg/kg *iv* as a pre-medication but may be titrated to the desired effect by incremental doses of 0.05 mg/kg<sup>[39]</sup>.

Opioids are potent analgesics which express their activity *via* different opioid receptors. The most suitable for sedation is fentanyl due to its rapid onset and short action. As it has no sedation properties it must be combined with benzodiazepines but the combination increases the risk of respiratory depression<sup>[38]</sup>. Other undesirable effects are itching, hypotension and vomiting but those are less pronounced than in histamine-releasing opioids such as morphine and meperidine<sup>[38]</sup>. Naloxone is an opioid receptor antagonist and is administered intravenously at 0.1 mg/kg<sup>[38]</sup>.

Meperidine was the first synthetic opioid agent. It acts mainly as an antagonist of  $\mu$  and  $\kappa$  receptors and has an analgesic potency ten times greater than that of morphine<sup>[62]</sup>. Like other opioid drugs, meperidine causes nausea, vomiting, urinary retention and respiratory depression. Its property of acting on nerve fibers, similar to those of local anesthetics, allows its use as an alternative for anesthetic blockade and differentiates it from other opioids. An *iv* route has been used for treating moderate to severe pain, for regional anaesthesia, for pre-medication and for analgesia during anesthesia. The combination of midazolam and meperidine can be used to achieve sedation and analgesia during colonoscopy<sup>[63]</sup>. There are few studies that have compared the efficacy of midazolam alone to midazolam and meperidine. According to Ozel *et al*<sup>[64]</sup>, there were no significant differences in oxygen saturation/blood pressure but a better patient compliance was observed in the combined sedation group<sup>[64]</sup>. Cinar *et al*<sup>[65]</sup> showed that in respect of the recovery and procedure time there were no significant differences between the midazolam and the midazolam/meperidine group<sup>[65]</sup>. In a randomized trial comparing the efficacy and recovery time of two sedation

regimens consisting of midazolam in combination with either meperidine or fentanyl, it was found that the fentanyl combination with midazolam resulted in a significantly faster recovery, without any apparent loss of analgesic effect<sup>[66]</sup>. Again, these are adult studies, and extrapolation to pediatrics is not necessarily appropriate.

Meperidine is administered intravenously at 1 mg/kg<sup>[64]</sup>. A possible flow chart of benzodiazepine and opioid sedation for pediatric GI endoscopy is presented in Figure 3.

Fentanyl is usually administered at 1–2  $\mu$ g/kg. The analgesic effect lasts 20–40 min<sup>[38]</sup>.

van Beek and Leroy<sup>[2]</sup>'s analysis found opioid and benzodiazepine sedation protocols suboptimal. These protocols were inferior in comparison to general anaesthesia. The comparison of midazolam/fentanyl with propofol sedation by Lightdale *et al*<sup>[67]</sup> addressed mainly procedure duration and discharge times which were similar for both groups, but the endpoint of this study was not to compare safety or efficacy.

### **Inhalation anesthetics**

In most countries, legislation limits the administration of inhalation anesthetics to anesthesiologists.

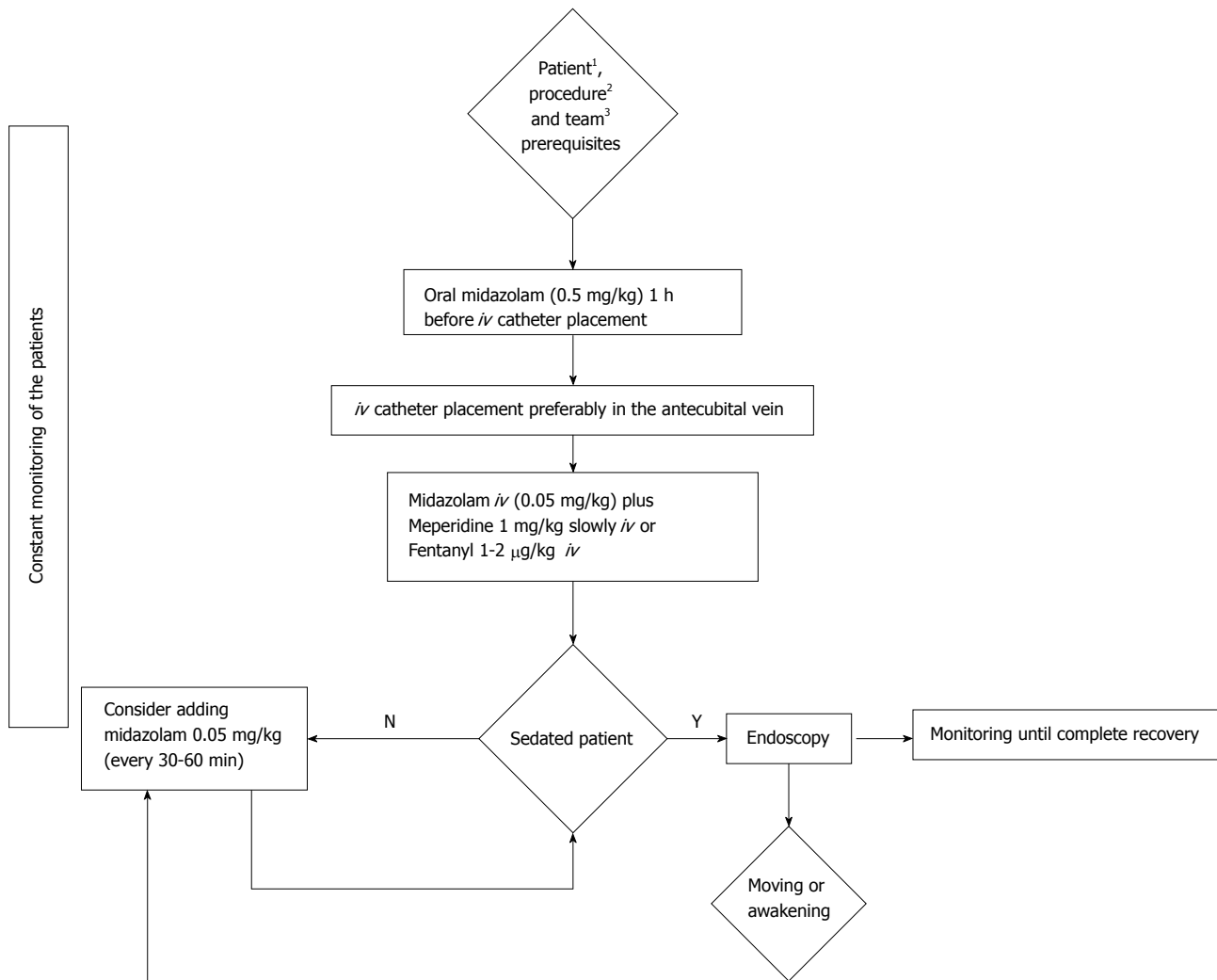
**Sevoflurane:** Sevoflurane is an inhalational anesthetic with a very good safety profile (low incidence of airway hypersecretion, respiratory depression or cardiovascular events)<sup>[47]</sup>. When used for paediatric sedation for endoscopies it was characterized by a shorter recovery time and earlier discharge. Sevoflurane can only be administered by an anesthesiologist. The insertion of an *iv* catheter may not be needed. The use of inhaled anesthetics requires waste gas scavenging to prevent anesthetic gases being released into the ambient air<sup>[47]</sup>.

There are no recently published studies on sevoflurane sedation for pediatric GI endoscopies.

**Nitrous oxide:** Nitrous oxide is an inert gas which has analgesic, sedative and amnesic properties of short duration. Michaud *et al*<sup>[68]</sup> reported a good experience with 50% nitrous oxide for gastroscopies and proctosigmoidoscopies in children. They did not evaluate it for ileo-colonoscopy nor compare this type of sedation to other protocols<sup>[68]</sup>. There are no newer studies on nitrous oxide sedation for GI endoscopy in children.

In adults nitrous oxide has been used successfully for proctoscopies and colonoscopies. In a systematic review Welchman *et al*<sup>[45]</sup> analyzed in a systematic review 11 studies including 623 patients. Continuous nitrous oxide inhalation provided comparable analgesia to *iv* sedation for colonoscopies. There was no difference in procedural pain between on-demand nitrous oxide and no sedation for colonoscopies. The recovery time was shorter in the nitrous oxide groups<sup>[45]</sup>.

Nitrous oxide is often more used as an anxiolytic before *iv* catheter placement if the face mask does not agitate the patient. However, most anesthesiologists



**Figure 3** Flow chart of opioid and benzodiazepine sedation protocol for paediatric endoscopy. <sup>1</sup>Patient without contraindications (not being simultaneously treated with monoamine oxidase inhibitors); <sup>2</sup>Diagnostic endoscopy or procedure for which no endotracheal intubation is needed; <sup>3</sup>The team qualified for paediatric sedation for gastrointestinal endoscopy.

would suggest that age-appropriate calming of a patient by engagement would have a similar result. Vomiting occurs in up to 10%. It is contraindicated in bowel obstruction and should not be administered if any of the team members is pregnant<sup>[38]</sup>. Its routine use in pediatric GI endoscopy is not ratified.

#### Adjuvant medicines and antagonists

**Anti-cholinergics:** As discussed in the section on ketamine, anti-cholinergics (e.g., atropine or glycopyrrolate) decrease the hypersalivatory effect which may influence airway patency<sup>[59]</sup>. However, importantly, it should be noted that available evidence does not support this practice and anti-cholinergics are no longer routinely recommended<sup>[26,60]</sup>.

**Anti-emetics:** Many sedative/analgesic agents (e.g., ketamin, fentanyl), with the exception of propofol, provoke vomiting<sup>[50]</sup>. Ondansetron reduced the incidence of vomiting in a double-blind, randomized, placebo-controlled study in 255 children in an emergency depart-

ment sedated by ketamine<sup>[61]</sup>.

**Flumazenil:** Flumazenil is an antagonist used to reverse the undesirable effects of benzodiazepines such as respiratory depression. It is delivered *iv* at 0.1 mg/kg up to a maximum of 2 mg and has a rapid onset of action in 1-3 min. The half-life of flumazenil is shorter than that of other benzodiazepines (e.g., midazolam) making close monitoring essential and reapplication sometimes needed<sup>[38,40]</sup>.

**Naloxone:** Naloxone reverses opioid effects and results in normal respiration within 1-2 min of application of 0.1 mg/kg (up to 2 mg) *iv* or intramuscular. Its duration of action is around 20-40 min hence repeated doses might be needed as the duration of action of most opioids (e.g., fentanyl) is longer<sup>[38,40]</sup>.

## DISCUSSION

Effective and safe sedation for pediatric endoscopic proce-



dures is a non-negotiable pre-requisite and an important factor for lowering patient distress. In principle, total *iv* anesthesia should be performed by anesthesiologists. However, it has to be recognized that in many countries, including a majority of European countries and in parts of the United States, the limited availability of anesthesiology teams and limited organizational considerations represents a medical dilemma. In many European countries anesthesia departments cannot cope with the increasing demands<sup>[37]</sup>. Therefore, a shortage of anesthetic teams may force pediatric endoscopists to conduct sedation without anesthetic teams applying guidelines adapted according to national regulations and institutional practices<sup>[4]</sup>. However, this situation is not optimal and requires consequent actions to increase the number of anesthesiologists.

In this situation, the intention of the authors is not to encourage such practice. This paper summarizes the evidence for sedation schemes which could be safely and efficiently performed by non-anesthesiologists. Sedation protocols have to be adapted to international, national and local legislation and institutional practice. The national institutions must organize multidisciplinary teams for education, licensing and supervision of non-anesthesiologists and registered nurses involved in sedation practices as long as there is a shortness of anesthesiologists. An efficient system of quality control is a paramount.

The choice of medicines for procedural sedation is wide, but none has the properties of an ideal sedative, which are: predictable dose dependent level of sedation with rapid onset; broad therapeutic window; anxiolytic effect with anterograde amnesia for the duration of the procedure; absence of respiratory, cardiovascular and other undesirable effects; and a smooth post-procedural recovery without side effects<sup>[34]</sup>. Another important problem in pediatrics is the off-label use of many medicines, which was recently addressed for medicines prescribed for outpatients in pediatric gastroenterology<sup>[69]</sup>. The investigators found that in 33.2% of the prescriptions, medicines were used "off-label" and that 47.3% of the patients had at least 1 medicine described as an "off-label" medication. Sedatives and other *iv* medicines were not covered by this study. The legal risk of a prescribing doctor is greater when using "off-label" medicines or indications. Parents should be informed of the "off-label" use. A solution of this problem is to motivate the pharmaceutical companies to register medicines for pediatric use, as has happened in the majority of the EU Countries under the jurisdiction of the European Medical Agency for new medicines.

Propofol is probably the most promising and controversial sedative/anesthetic at present. It is stated that only those trained in anesthesia should use it, a position that anesthesiologists and their societies strongly defend<sup>[70]</sup>. On the other hand, there are studies of safe and efficient use of propofol for sedation for GI endoscopic investigations in pediatric and adult gastroenterology<sup>[2,3,7,8,51,71]</sup>. The administration of propofol

by non-anesthesiologists is "off-label" in most cases and, therefore, every adverse event might have medico-legal consequences.

Therefore, these data could not be simply extrapolated to every sedation/analgesia practice. According to the review by Havidich *et al*<sup>[72]</sup> the evidence of the safety of sedation by non-anesthesiologists for procedures outside operating theatres is growing, especially for propofol. Despite the drawbacks listed above, published data justify propofol use in certain circumstances<sup>[2]</sup>.

Ketamine-based sedation is safe and effective in otherwise healthy infants older than 3 mo<sup>[27]</sup>. Ketamine has dissociative anesthetic and analgesic properties with a wide safety margin and is frequently used in pediatric emergency departments<sup>[27,28]</sup>. Emergence reactions are observed in adults in up to 28%, but seem less prevalent in paediatric studies and not influenced by the addition of midazolam to ketamine<sup>[56-58]</sup>. Guidelines advised against routine benzodiazepine pre-medication<sup>[27,28]</sup>. Data from larger studies are needed as one recent study found less emergence reactions when midazolam was routinely administered as a pre-medication<sup>[4]</sup>. Another major limitation of ketamine-based sedation for endoscopy is laryngospasm. In general, the laryngospasm resolves without consequences rapidly after removal of the endoscope and administration of oxygen<sup>[73]</sup>. Another study reports transient laryngospasm manageable with simple measures in 3% of gastroscopies<sup>[4]</sup>. Therefore, the ketamine-based sedation regime for GI endoscopy is an acceptable option when sedation with propofol is not feasible.

Midazolam is most likely the most widely used drug for sedation in everyday endoscopic work. The duration of action of midazolam is dependent on the duration of its administration. The sedative and amnestic effects of benzodiazepines sometimes do not provide adequate patient comfort during colonoscopic procedures<sup>[74]</sup>. Opioids are often added and meperidine is commonly used<sup>[75]</sup>. The value of adding analgesics to sedatives has well evaluated in large number of prospective, randomized and placebo-controlled studies<sup>[76]</sup>. Sedation with midazolam/meperidine is safely and can be administrated under adequate monitoring<sup>[77]</sup>.

These recommendations review and discuss sedation practices for pediatric GI endoscopy which can be safely and efficiently performed by non-anesthesiologists, but only when the necessary pre-requisites regarding patient assessment, team composition and experience, medicines and equipment are met.

## ACKNOWLEDGMENTS

The authors reviewed the literature and made practical recommendations for effective and safe sedation for endoscopic procedures in children. However, the authors decline every legal responsibility for the proposed algorithms. Legislation and regulation regarding limitations of administration of different medications, such as inhalation anesthetics, differ from country to country.

Therefore, limitations caused by local legislation should be carefully checked.

## COMMENTS

### Background

Anesthesia is by preference performed by anesthesiologists.

### Research frontiers

The creation of sedation teams led by non-anesthesiologists and a careful selection of anesthetic drugs may offer an alternative, but should be in line with national legislation and institutional regulations.

### Innovations and breakthroughs

The intention of this review is to offer effective and safe alternatives for non-anesthesiologists.

### Peer-review

The present paper was well organized and well investigated. This paper will give us important information about the anesthesia during endoscopy especially in children.

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